

AMENDMENTS TO THE SPECIFICATION

At page 11, lines 14-17, please delete the entire paragraph and insert therefor the following paragraph:

B<sup>1</sup>  
--Figure 9 demonstrates *PTTG* mRNA expression and hydrocortisone. PHA (5 µg/mL)-stimulated normal adult human T<sub>2</sub>-cells were treated with hydrocortisone for 72 hours. *PTTG* mRNA of the T-cells was measured with northern blotting and percentage of the T-cells in S or G2/M phase was determined by FACS.--.

At page 11, lines 18-20, please delete the entire paragraph and insert therefor the following paragraph:

B<sup>2</sup>  
--Figure 10 shows *PTTG* mRNA expression and cyclosporin. PHA (5 µg/ml)-stimulated normal adult human T<sub>2</sub>-cells were treated with cyclosporin for 72 h. ~~*PTTG*~~ *PTTG* mRNA of the T-cells was measured with northern blotting and percentage of the T-cells in S or G2/M phase was determined by FACS.--.

At page 11, lines 21-23, please delete the entire paragraph and insert therefor the following paragraph:

B<sup>3</sup>  
--Figure 11 illustrates *PTTG* mRNA expression in leukemia cells. *PTTG* mRNA values and cell cycle of cycling human leukemia HL-60 (column 1), Jurkat T cells (column 2), resting cells (column 3), PHA (5 µg/mL)-stimulated, (column 4) anti-CD3-stimulated, and (column 5) normal adult human T cells were determined.--.

At page 11, lines 24-28, please delete the entire paragraph and insert therefor the following paragraph:

B4  
--Figure 12 shows PTTG mRNA expression and cell cycle in T<sub>h</sub>-cells. T<sub>h</sub>-cells were treated with the following conditions and PTTG mRNA and percentage of S phase were compared. (column 1) resting T<sub>h</sub>-cells; (column 2) PHA (5 µg/mL)-stimulated T<sub>h</sub>-cells; (column 3) anti-CD3-stimulated T<sub>h</sub>-cells; (column 4) anti-CD3 + hydrocortisone (100 nM)-treated T<sub>h</sub>-cells; (column 5) anti-CD3 + cyclosporine A (1 µg/mL)-treated T<sub>h</sub>-cells; (column 6) anti-CD3 + aphidicolin (1 µg/mL)-treated T<sub>h</sub>-cells; (column 7) anti-CD3 + nocodazole (500 ng/mL)-treated T<sub>h</sub>-cells; (column 8) anti-CD3 + TGF-β1 (10 ng/mL)-treated T<sub>h</sub>-cells.--.

At page 11, line 29 through page 12, line 4, please delete the entire bridging paragraph and insert therefor the following paragraph:

B5  
--Figure 13 shows PTTG mRNA expression in human Jurkat T<sub>h</sub>-cell leukemia line. Jurkat T<sub>h</sub>-cells were treated as described below. (column 1) Jurkat cells kept for 48 h in 1% FBS-supplemented culture medium; (column 2) Jurkat cells after medium change for fresh 1% FBS-supplemented; (column 3) Jurkat cells after medium change for 10% FBS-supplemented; (column 4) Jurkat cells after medium change with phytohemagglutinin (PHA; 1 µg/mL) + phorbol-12-myristate-13-acetate (PMA; 50 ng/mL) in 1% FBS; (column 5) Jurkat cells after medium change with (PHA + PMA) + cyclosporine A (1 µg/mL); (column 6) Jurkat cells after medium change with (PHA + PMA) + TGF-β1 (10 ng/mL).--.

At page 82, line 27 through page 83, line 9, please delete the entire bridging paragraph and insert therefor the following paragraph:

B6  
--We found that CD3 antibody-induced activation of T-cells was inhibited to different extents by cyclosporin A, hydrocortisone, aphidicolin (S phase inhibitor), or nocodazole (G2/M phase blocker), while TGF- $\beta$ 1 (10 ng/mL final concn) had no significant effect neither on *PTTG* mRNA nor on the amount of S- or G2/M-phase cells (Figure 12). At the same time, neither fresh 1% or 10% FBS nor a ~~mixture~~ mixture of phytohemagglutinin (PHA) and phorbol-12-meristate-13-acetate (PMA) [i.e., PHA+PMA mixture] considerably elevated *PTTG* level in Jurkat T-cell line and this mixture even decreased it. Jurkat cells were used for comparison and they were treated with PHA+PMA mixture which is used for its mitogenic action for Jurkat T-cells after being cultured for 48 hours in 1% FBS-supplemented medium. Changes in the amount of S-phase cells were also parallel to changes in the level of *PTTG* mRNA expression. Cyclosporin A and TGF- $\beta$ 1 decreased both *PTTG* mRNA level and the amount of S-phase Jurkat cells, while hydrocortisone did not change these indexes even used in 10  $\mu$ M final concentration (data are not shown).--.

At page 84, lines 7-11, please delete the entire paragraph and insert therefor the following paragraph:

B7  
--While the present invention is not committed to or dependent any particular mechanism of action, *PTTG* mRNA induction and parallel S-phase increase during normal T-cell activation imply that the mechanism of *PTTG* cell transforming action could be in its overexpression and resulting increase in cell cycling rather than in its misregulating effect on ~~chromatide~~ chromatid separation and resulting aneuploidy.--.